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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,894	11/21/2003	Dominic Zichi	SML.10	1434

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,894	ZICHI ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 13-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 21 December 2007 has been entered.

Claims 13-17 are newly added. Claims 11 and 12 have been cancelled. Claims 1-10 and 13-17 remain in the case.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-10 and 13-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope with these claims.

Applicant teaches detection of protein analyte bound to a (photocrosslinking) nucleic acid ligand with universal protein stains, in particular after photocrosslinking of analyte and nucleic acid ligand and stringent washing (see e.g. [0034]; or, US 6,242,246, cols. 10-17; or, US 6,544,776, cols. 10-18). Applicant provides no description or guidance for detection with protein stains other than with aptamer capture reagents. Applicant also teaches that stringent washing conditions are needed to remove non-specifically bound proteins. In the absence of further written description and guidance from applicant, one would not be guided to, or assured of the ability to, detect a protein analyte bound to a protein capture reagent with a protein stain or to use other than stringent washing conditions with an analyte bound to a nucleic acid ligand.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 10, and 13-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and claims dependent thereupon, the interrelationships of the components and steps of the method are not clear, e.g. it is not clear what amount of first analyte is detected, the amount in the biological fluid or the amount capable of binding to the solid support.

In claims 10 and 15 it is not clear what is encompassed by a "universal protein stain."

Claims 14 and 15 are method claims and, as such, they should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as mixing,

reacting, and detecting. A "use" is not a valid method step. Moreover, it is believed -- performed-- was intended in claim 15.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 9, and 13-15 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Chandler et al. (US 6,449,562).

Chandler et al. teach multiplexed assays for determination of reagent binding wherein unlabeled ligand binding partners are added ("spiked") to the reaction of immobilized ligand binding partners and a soluble ligand (see e.g. cols. 24-27). Binding of the labeled soluble ligand to the immobilized ligand binding partners was determined.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
(c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1, 3-10, and 14-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gold et al. (US 6,458,539) in view of Lin et al. (US 2002/0037506) and Graham et al. (US 4,743,542).

Gold et al. teach methods using nucleic acid ligand diagnostic biochips in which a sample containing unknown protein substances is applied to a solid support containing immobilized photoaptamers specific for many different marker proteins and the protein substances are detected after binding, cross-linking, and washing with a universal protein stain binding to amino acids. However, the reference does not discuss methods to deal with large concentrations of a protein substance which saturates the binding of the immobilized aptamers.

Lin et al. teach that binding assays using aptamers are, as antibody-based assays, subject to the saturation of the binding capacity of the binders, particularly in sandwich assays producing the notoriously old and well known hook effect (see ¶¶ [0016] and [0059]). However, the reference does not teach methods to reduce the saturation and, if a sandwich assay, the hook effect.

Graham et al. teach increasing the dynamic range of an immunoassay and forestalling the hook effect caused by saturation of (filling of) immobilized ligand binding partners by addition of unlabeled ligand binding partners to a solution containing sample.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have reduced the saturation of binding sites in aptamer-based assays as taught to occur in Lin et al. with the addition of unlabeled ligand binding partner, as taught in

Graham et al., in the aptamer-based assays of Gold et al., as was well known in the art. One would have had a reasonable expectation that the known methods would successfully reduce the saturation effect and increase the measuring range of the assay regardless of the nature of the ligand binding partner in view of the comparability of aptamer-based and antibody-based assays taught in Lin et al.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claims 5-8 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Chandler et al. (US 6,449,562), if necessary in light of applicant's disclosure.

The teachings of Chandler et al. are as set forth previously in this Office action. However the dissociation constant and the relative concentration of the ligand binding partners could not be determined from the disclosure of the reference. Inherently, the parameters fall within the ranges as claimed based on the shifts in the standard curves noted in the reference. If not, in light of applicant's calculations, it would have been implicit to have adjusted the concentration of the ligand binding partner in solution to the ranges as claimed to provide a usable standard curve in the method.

Claims 1, 3-9, 14, 16, and 17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lin et al. (US 2002/0037506) in view of Graham et al. (US 4,743,542) for reasons of record.

Applicant's arguments filed 21 December 2007 have been fully considered but they are not deemed to be persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a non-sandwich assay) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Notwithstanding applicant's assertions to the contrary, applicant's open claim language does not exclude additional reagents for detecting bound analyte. Indeed, applicant incorporates the disclosures of U.S. Pat. Nos. 6,242,246 or 6,544,776 which disclose sandwich assays for detection (see e.g. cols. 10-11).

In response to Applicant's arguments that there are no specific suggestions to combine the references, the examiner recognizes that references cannot be arbitrarily combined and that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the common knowledge or common sense generally available to one of ordinary skill in the art. See: *In re Nomiya*, 184 USPQ 607 (CCPA 1975); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); or, *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). However, there is no requirement that the claimed invention or a motivation to make the modification be expressly articulated in any one or all of the references. The test for combining references is what the combination of disclosures, taken as a whole, would suggest to one of ordinary skill in the art. See: *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); or, *In re McLaughlin*, 170 USPQ 209 (CCPA 1971). References

are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. See: *In re Bozek*, 163 USPQ 545 (CCPA 1969). A person of ordinary skill in the art, using common knowledge and common sense, is capable of fitting the teachings of multiple references together like pieces of a puzzle, regardless of the specific problem being addressed by the individual references. Any need or problem known at the time of the invention can provide a reason for combining elements of the different references. A person of ordinary skill in the art is also a person of ordinary creativity. In this case, for the reasons of record, ample motivations to combine the references with an extremely reasonable expectation of success have been set forth. As set forth, one would have had a reasonable expectation that the known method of adding unlabeled ligand binding partner, as taught in Graham et al. would successfully reduce the saturation effect (the hook effect in a sandwich assay) and increase the measuring range of the assay regardless of the nature of the ligand binding partner in view of the comparability of aptamer-based and antibody-based sandwich assays taught in Lin et al.

Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
March 27, 2008

/Long V Le/
Supervisory Patent Examiner, Art Unit 1641